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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/620,586 | 07/20/2000 | Steen Klysner | 0459-0464P | 2471 |

2292 7590 04/08/2003

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| EXAMINER |
|---|
| BELYAVSKYI, MICHAIL A |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1644 | 18 |

DATE MAILED: 04/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/620,586 | KLYSNER ET AL. | |
| | Examiner | Art Unit | |
| | Michail A Belyavskyi | 1644 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *3/29/02;8/05/02;12/03/02* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-56* is/are pending in the application.

4a) Of the above claim(s) *8,12-15,18,24-28 and 30-52* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7,9-11,16,17,19-23,29 and 53-56* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 July 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *5,6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Claims 1-56 are pending.

2. Applicant's election of Group I (claims 1-23 and 29), now claims 1-23, 29 and 53-56 , i.e. a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof , or at least one GDF-8 analogue wherein the analogue has been modified so that at least one foreign $T_H$ epitope moiety (A) is introduced and wherein T cell epitope is *Tetanus toxoid* epitope and species identified as without a carrier molecule in Paper NO: 9, filed 03/29/02, and the election of species B of the item 5.4 (modification by substituting at least one amino acid) and bovine GDF-8 as species of GDF-8 in Paper NO:12, filed on 08/05/02 and the election of species B of the item 5.4.1( SEQ ID NO:12 as a specific species to be modified by substituting) and the species D of the item 5.4.2.1 ( a specific position of substituted amino-acid from 49-69) in Paper NO: 15 are acknowledged.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 24-28 and 30-52 (non-elected groups II-XCIV) and claims 8, 12-15 and 18 (non-elected species of elected group I) are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-7,9-11, 16-17, 19-23, 29 and 53-56, read on a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or fragment thereof , or at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is *Tetanus toxoid* epitope is introduced without a carrier molecule, and wherein modification is substitution in SEQ ID NO:12 at amino acid from 49-69 are under consideration in the instant application.

3. The specification is objected to under 37 CFR 1.821(d) for failing to disclose SEQ ID NOS, for the amino acid sequence disclosed on page 43, lines 2 and 3.

4. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Denmark on 07/20/1999. It is noted, however, that applicant has not filed a certified copy of the 1999 01014 application as required by 35 U.S.C. 119(b).

5. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

6. The use of the trademark " ISCOM" has been noted in this application (page 33, line 17). Each letter of the trademarks should be capitalized wherever it appears and be accompanied by the generic terminology.
Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

7. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP□ 608.01(o). Correction of the following is required:

Applicant is requested to identify the written support for claims 23, particularly the claimed limitations of " the GDF-8 polypeptide is contained in a virtual lymph node device. Alternatively, Applicant is invited to amend the specification to provide antecedent basis for the claimed subject matter.

8. The following is a quotation of the second paragraph of 35 U.S.C. 112.

> *The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.*

9. Claims 2-7, 9-11, 23 and 55 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claim 2 is indefinite and ambiguous in the recitation of "the method according to claim 1, wherein is presented …". It is unclear what Applicant mean by this phrase " ?

B. Claim 4 is indefinite and ambiguous in the recitation of "suitable chemical groups". The characteristics and metes and bounds of these "suitable chemical groups" are unclear and indefinite.

C. Claim 23 is indefinite and ambiguous in the recitation of "virtual lymph node device". The characteristics and metes and bounds of "virtual lymph node device" are unclear and indefinite.

D. Dependent claims 55 recites "natural T cell epitope". There is insufficient antecedent basis for this limitation in the claims, since base Claim 1 does not recite "natural T cell epitope".

10. The following is a quotation of the first paragraph of 35 U.S.C. 112:

*The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.*

11. Claims 1-7, 9-11, 16-17, 19-23, 29 and 53-56 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide of SEQ ID NO:12, or at least one GDF-8 analogue thereof, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analogue has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is *Tetanus toxoid* epitope is introduced without a carrier molecule, and wherein the modification is substituted in SEQ ID NO:12, does not reasonably provide enablement for on a method for in vivo down-regulation of GDF-8 comprising administering *any* fragment of GDF-8 polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

The instant claim encompass fragments. There is insufficient guidance and direction as to how to make and use *any* fragments of GDF-8 polypeptide that can induces production of antibody against the GDF-8 polypeptide. There is insufficient guidance as to which amino acid residue within the GDF-8 polypeptide, encoded by SEQ ID NO:12 can be deleted, substituted and whether the resulting resulting polypeptide would maintain the same function as polypeptide, encoded by SEQ ID NO: 12. Moreover, Applicant acknowledge that not all variants or

fragments of native GDF-8 polypeptide will have the ability to elicit antibody which are cross-reactive with the native form (see page 51, lines 4-8 in particular).

Colman *et al.,* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al.,* in Journal of Protein Chemistry (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Further, Lederman *et al* in Molecular Immunology (28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). In addition, the current state of the art in epitope structure prediction is limited given the noncontiguous amino acid residues constitute most epitopes, and that the dynamics of binding is often not integrated into the epitope prediction equation, making epitope structure prediction a complex four-dimensional problem (see Van Regenmortel, page 464, abstract in particular; Methods: A Companion to Methods of Enzymology 9:465-472, 1996). Van Regenmortel notes that 90% of antibodies raised against intact proteins do not react with any peptide fragment derived from the parent protein indicating that these antibodies are directed to discontinuous epitopes (see page 466, column 1 in particular). In addition Van Regenmortel states that the low success rate of antigenic prediction is due to the fact that predictions concern only continuous epitopes and it is unrealistic to reduce the complexity of epitopes that always possess conformational features to one-dimensional, liner peptide models (see page 467, column 2 in particular). Detailed information regarding to how to make and use any fragments of GDF-8 polypeptide that can induces production of antibody against the GDF-8 polypeptide is lacking. Therefore, predicting which antibodies outside of the antibodies to GDF-8 polypeptide or to at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is Tetanus toxoid epitope in a method for in vivo down regulation of GDF-* activity is well outside the realm of routine experimentation. A skilled artisan would require guidance, such as information regarding the specific epitope recognition of the antibodies successfully used in the instant invention in a manner reasonably commensurate with the scope of the claims. Thus, it would require undue experimentation of one skilled in the art to practice the claimed invention.

The scope of the claimed method for in vivo down-regulation of GDF-8 comprising administering any fragment of GDF-8 polypeptide is not commensurate with the enablement provided by the disclosure a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analoge has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is Tetanus toxoid epitope is introduced without a carrier molecule, and wherein modification is substitution in SEQ ID NO:12 at amino acid from 49-69 with regard to the extremely large number of amino acid sequences broadly encompassed by the claimed invention. Since the amino acid sequence of a

protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's or peptide's amino acid sequence, and, in turn, nucleic acid sequence and still retain similar biological activity or structural specificity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the protein's structure relates to its function. However, the problem of predicting protein structure from mere sequence data of a limited number of proteins and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein and finally what changes can be tolerated with respect thereto is extremely complex and well outside the realm of routine experimentation.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method for in vivo down-regulation of GDF-8 comprising administering *any* fragment of GDF-8 polypeptide in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

12. Claims 1-7, 9-11, 16-17, 19-23, 29 and 53-56 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is in possession of : a method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide of SEQ ID NO:12, or at least one GDF-8 analogue thereof, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analogue has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is *Tetanus toxoid* epitope is introduced without a carrier molecule, and wherein the modification is substituted in SEQ ID NO:12.

Applicant is not in possession of : a method for in vivo down-regulation of GDF-8 comprising administering any fragment of GDF-8 polypeptide.

The specification fails to define any fragments of GDF-8 polypeptide that can be used to induces production of antibody against the GDF-8 polypeptid. Moreover, there is insufficient guidance as to which amino acid residue within the GDF-8 polypeptide, encoded by SEQ ID NO:12 can be deleted, substituted and whether the resulting resulting polypeptide would maintain the same function as polypeptide, encoded by SEQ ID NO: 12 .
Applicant has disclosed a limited number of species; therefore, the skilled artisan cannot envision all the contemplated amino acid sequence possibilities recited in the instant claims. Consequently, conception in either case cannot be achieved until a representative description of the structural and functional properties of the claimed invention has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The sequences themselves are required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993).

A description of a genus of protein sequences may be achieved by means of a recitation of a representative number of polypeptide sequences, defined by amino acid sequence, falling within the scope of the genus, or of a recitation of structural features common to the genus, which features constitute a substantial portion of the genus. Regents of the University of California v. Eli Lilly&Co., 119F3d 1559, 1569, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the written description inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.). Consequently, Applicant was not in possession of the instant claimed invention. See University of California v. Eli Lilly and Co. 43 USPQ2d 1398.

Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

13. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

*(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.*

14. Claims 1-2, 16, 19, 22,29, 53, 54 and 56 are rejected under 35 U.S.C. 102(e) as being anticipated by Barker et al.(US. Pat. No. 6,369,201, see entire document).

US Patent '201 teaches a method for in vivo down-regulation of myostatin (GDF-8) activity, which will result in increase in muscle mass of an animal, comprising administering at least one full length myostatin polypeptide, or at least one myostatin analogue, wherein myostatin is derived from bovine and myostatin immunoconjugate comprising at least one myostatin polypeptide, linked to an immunological carrier (see Abstract and Column 4, especially lines 1-4; column 7 lines 15-22, column 9, lines 22-35, column 13, lines 1-5 in particular). It is noted that US Patent '201 teaches SEQ ID NO:2 that is 100 % identical to SEQ ID NO:12 of the instant application. ( see sequence alignment) US Patent '201 teaches that the term "myostatin immunogen" includes polypeptide of myostatin molecule, analogue and modification by substitution such that a substantial fraction of myostatin B cell epitopes are preserved and do not affect the ability of the analog to induces an immunological response (see column 6, lines14-65, column 7, lines 6-15, column 15 lines 1-5, and column 16, lines 42-45 in particular). US Patent '201 teaches a myostatin multimer, wherein modification includes duplication of at least one myostatin B cell epitope ( see column 7, lines 23-30 and column 8, lines 45-65 in particular). US Patent '201 teaches modification of miostation to include vaccine composition comprising the myostatin polypeptide or analogue and formulated with various adjuvants , such as aluminum adjuvant ( see column 24, lines 1-20 in particular) and "immunological carriers" , such as *Tetanus toxoid* epitope, that will enhance the immunogenicity to the molecule and which facilitates breaking of autotolerance (see Column 4, line 10-15, column 9, lines 20-45 in particular). US Patent '201 teaches various method of administering myostatin-containing formulation, including parenteral route ( see column 25). US Patent '201 teaches that effective dosages can be readily established by one of ordinary skill in the art through routine trials ( see column 25, line 54-56 in particular).

Claim 29 is included because the claimed functional limitation would be inherent properties of the referenced method in vivo down-regulation of myostatin (GDF-8) activity, which will result in increase in muscle mass of an animal, because the reference method using the same method steps and ingredients as the claimed method. Under the principles of inherency, if a prior art method, in its normal and usual operation, would necessarily perform the method claimed, then the method claimed will be considered to be anticipated by the prior art. When the prior art method is the same as a method described in the specification, it can be assumed the method will inherently perform the claimed process. See MPEP 2112.02.

The reference teaching anticipates the claimed invention.

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

16. Claims 1-7, 9, 10, 11, 16, 17, 19, 20, 21, 23 and 55 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barker et al.(US. Pat. No. 6,369,201) in view of the known fact disclosed in the specification on page 16, lines 24-30.

The teaching of US Patent '201 has been discussed, supra. US Patent '201 further teach that in order to facilitate breaking of autotolerance to autoantigens myostatin molecule can be modified by association with *Tetanus toxoid* epitope ( see column 9, lines 20-45). US Patent '201 does not explicitly teaches the particular modification of myostatin wherein said molecule has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is *Tetanus toxoid* epitope is introduced at amino acid from 49-69 of myostatin SEQ ID NO:12.

The Known fact disclosed that it is well know in the art various methods of modifying a peptide self-antigen in order to obtain breaking of autotolerance, including introducing into said molecule at least one foreign T cell epitope such *Tetanus toxoid* P2 and P30 epitopes. ( see page 16, lines 24-30).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to apply the teaching of the known fact disclosed in the Specification on page 16, lines 24-30 to those of US Patent '201 to obtain a claimed method for in vivo down-regulation of GDF-8 comprising administering at least one GDF-8 polypeptide, or at least one GDF-8 analogue, wherein GDF-8 is derived from bovine GDF-8 polypeptide and wherein the analogue has been modified so that at least one foreign $T_H$ epitope moiety, wherein T cell epitope is Tetanus toxoid epitope is introduced without a carrier molecule, and wherein modification is substitution in myostatine molecule of SEQ ID NO:12 at amino acid from 49-69.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because it well know in the art that modifying a peptide self-antigen by including introducing into said molecule at least one foreign T cell epitope ( *Tetanus toxoid* epitope ) will facilitates breaking of autotolerance, as taught by the Known fact disclosed in the Specification on page 16, lines 24-30 and can be further used in the method for in vivo down-regulation of myostatin (GDF-8) activity, taught by US Patent '201.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Claims 17 , 20, 21 and 23 are included because it would be conventional and within the skill of the art to : (i) identify the exact position for substitution for *Tetanus toxoid* epitope in myostatin molecule in order to facilitates breaking of autotolerance of said molecule; or (ii) determine an effective amount of myostatin polepeptide; or (iii) determine the optimum duration and means of administration. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

17. No claim is allowed.

18. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
April 7, 2003

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